to class-III EAD. *Methods:* Action potentials (AP) and contractions (indicating sarcoplasmic reticulum (SR) Ca^{2+} release) were recorded in canine left ventricular myocytes with microelectrodes at steady-state cycle lengths (CL) of 300 to 4000 ms. Threshold concentrations for EAD induction were for ISO: 20–50 nmol/L, ALMO: 3.0 μmol/L, *d*-SOT: 500 μmol/L. *Results:* ISO EAD (n_{cells} = 12; n_{dogs} = 7) were generated only at CL ≤ 1000 ms (peak incidence at CL = 500 ms: 3 EAD/10 AP) versus class-III EAD (n_{cells} = 6; n_{dogs} = 4) only at CL ≥ 2000 ms (peak at CL = 4000 ms: 4 EAD/10 AP). Prior to the occurrence of class-III EAD, APD_{95} had greatly increased compared to control. Prior to ISO EAD, APD_{95} showed relatively much less increase. ISO EAD, but not class-III EAD, were accompanied by aftercontractions. These 'early aftercontractions' started earlier than EAD upstrokes and occurred often in their absence, always before full repolarization of the AP. *Conclusions:* (1) ISO EAD are typically induced by fast pacing (CL ≤ 1000 ms) in contrast to class-III EAD. (2) Early aftercontractions precede ISO EAD but are not seen with class-III EAD. Our data provide strong support for the role of cellular Ca^{2+} overload and spontaneous SR Ca^{2+} release in the generation of ISO EAD and suggest that ISO EAD are mechanistically different from class-III EAD.

1019-98 Effects of Global Ischemia on Propagation During Ventricular Fibrillation in the Isolated Rabbit Heart

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Ventricular fibrillation (VF) leads to global ischemia of the heart. The effects of ischemia on cardiac excitation during fibrillation remain unclear. We hypothesized that global ischemia during sustained VF reduces cell excitability, leading to non-uniform decrease in conduction velocity (CV) and slowing of VF frequency, in spite of action potential duration (APD) decrease. The Langendorff-perfused rabbit heart was subjected to 15 min of no-flow global ischemia, followed by reperfusion, to study VF excitation patterns (n = 5). The perfused heart was immersed in Tyrode's saturated with 100% O_2 (control) or 100% N_2 (ischemia). Video imaging (~ 40,000 pixels per frame; 240 frames/sec) using a voltage sensitive dye, ECG and signal processing (Fast Fourier transform) were used for analysis. During VF, the dominant frequency decreased from 10.3 ± 1.7 Hz (mean ± SE) in control to 4.5 ± 0.6 Hz after 6–9 min of ischemia ($p < 0.03$). In addition, the spatial patterns of activation on the surface of the left ventricle and the ECG complexes became more organized in 3 of the experiments. The density of rotating waves decreased by 22 to 65%. These changes are attributed to increase in core size, as well as to decreases in CV and APD. Isochrone and APD maps obtained during constant pacing (cycle length, 200 msec) in the absence of VF (n = 5), confirmed that ischemia induces heterogeneous decreases in CV and APD that revert during reperfusion. Before ischemia, CV along longitudinal (V_L) and transverse (V_T) fiber axes was 1.0 ± 0.08 and 0.38 ± 0.04 m/sec respectively. After 6–9 min of ischemia, V_L and V_T decreased to 0.71 ± 0.06 m/sec ($p < 0.05$) and 0.12 ± 0.05 m/sec ($p < 0.01$), respectively. At this time there was bunching of isochrones in the transverse direction with occasional block leading to anisotropic reentry. APD decreased throughout the ventricular surface and there was an increase in APD dispersion at 10–15 min of ischemia. These results show that global ischemia alters activation patterns during VF, by decreasing excitation frequency, CV and APD, as well as core size and density of rotating waves.

1019-99 Demonstration of Sustained Reentry in the Mouse Heart

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We determined whether a critical size of cardiac tissue is necessary for the creation of a rotor or a mirror-image pair of rotors. The idea that fibrillation is only possible in hearts exceeding a critical mass was introduced over 80 years ago and has since been generally accepted. Recent estimates suggest that the critical size required for sustained reentry is about 100–200 mm^2. According to these estimates sustained reentry would not be possible in the mouse heart whose left ventricular area is approximately 20–30 mm^2. To test whether sustained reentry could be induced in such an area, we developed a technique that allows for recording of electrical activity on the epicardial surface of the Langendorff-perfused adult mouse heart. Measurements of conduction velocity (CV) and mean action potential duration (APD) were made using optical recording techniques and a voltage sensitive dye. CV decreased from 0.29 m/sec at a cycle length (CL) of 300 ms to 0.13 m/sec at a CL of 90 ms. Mean APD also showed CL dependence, decreasing from 69.5 ms to 52 ms at CL of 300 ms and 90 ms, respectively. Wavelength, estimated as the product of APD and CV, was 20 mm at 300 ms CL and 6.76 mm at 90 ms CL. In each case the wavelength was larger than the length of the heart (~6 mm). In 3 hearts, burst pacing near the apex of the left ventricle induced sustained reentrant activity. In two hearts sustained vortex-like reentry occurred around a single organizing center (core). The perimeter of the core was 3.36 mm^2. In another heart a mirror image pair of rotors was demonstrated. The period of rotation of these arrhythmias ranged from 50 to 66 ms. Our data show for the first time that the left ventricle of the mouse heart is capable of sustaining single or pairs of viable rotors. These data challenge the critical mass hypothesis by demonstrating for the first time that ventricular tissue with an area as small as 20–30 mm^2 is capable of undergoing sustained reentrant activity. The results further demonstrate that the wavelength during periodic stimulation is a poor predictor for initiation or maintenance of reentry in the mouse heart.

1019-100 Differential Effects of d,l-Sotalol and d-Sotalol on Isoprenaline Increased Delayed Rectifier Outward K^+ Current in Guinea Pig Myocytes. Beta-Adrenergic Blocking Property of D,l-Sotalol

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Catecholamines antagonize the clinical efficacy of pure class III antiarrhythmic agents in vivo. The class III antiarrhythmic agent d,l-sotalol (Sot) has significant β-adrenergic blocking property. However, its d-isomer without β-blockade has been shown to extert significant proarrhythmia. Thus, we compared the effects of Sot and d-sotalol (D-Sot) on delayed rectifier K^+ outward current in the presence of isoprenaline (ISO) at different concentrations. Time- dependent delayed rectifier K^+ outward currents, I_k (I_{kr} and I_{ks}) and tail current (I_{ktail}) were obtained in isolated guinea pig myocytes using the whole-cell patch clamp technique. Currents were measured in response to 300 ms depolarizing pulses from a holding potential of −40 mV in three experimental protocols [control, ISO (10^{-9}–10^{-6} M), and ISO (10^{-9}–10^{-6} M) plus either Sot (10^{-4} M) or D-Sot (10^{-4} M)]. I_{ktail} currents were measured upon repolarization to −40 mV. ISO significantly increased I_k and I_{ktail} in a dose-dependent manner. I_k was significantly amplified in the presence of ISO (10^{-9}–10^{-6} M) plus D-Sot. At 10^{-8} M ISO, I_k was increased by 92.3 ± 23.7% before and 54.3 ± 13.4% after D-Sot. In contrast, Sot strongly suppressed the effect of ISO on I_k, and compared to control, I_k was decreased by 35.6 ± 8.1% at 10^{-8} M ISO. D-Sot and Sot tended to reduce I_{ktail} at any concentrations of ISO compared to control, and the difference between drugs was not significant. The β-adrenergic blocking property of d,l-sotalol maintains delayed rectifier K^+ outward current block in the presence of ISO in guinea pig myocytes. This may explain its superior antiarrhythmic efficacy compared to d-sotalol.

1019-101 Evolving Electrophysiologic Heterogeneity in Experimental Myocardial Infarction

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To examine changes in the heterogeneity of electrophysiologic properties as canine MI heals, 18 dogs were studied. Six were normal dogs, 6 dogs were studied 5 days after LAD occlusion and 6, 8 weeks after MI. Electrophysiologic properties were evaluated with a 112 electrode plaque on the anterior LV including pacing threshold (TH), refractory period (ERP), activation-recovery times (ART), longitudinal conduction velocity, and a new index of heterogeneity of conduction based on the deviation of propagation from an anisotropic model (CHI). Heterogeneity was characterized locally and globally (SD under the entire plaque in each dog).

Results: Mean global parameters are shown in the first 4 columns of the table.

Dispersion (SD over plaque)

	Threshold (mA)	ART (ms)	ERP (ms)	ERP/ART	Velocity (m/sec)	CHI
Normal	0.66	11.6	7.2	0.079	0.46	3.2
5 Day	1.40*	24.5*	21.6*	0.200*	0.46	4.6
8 Week	0.86	15.2	11.5	0.094	0.37*	5.2*

*$p < 0.05$ vs normals

Local and global changes behaved similarly. ERP and ART were moderately correlated in normal (R = 0.54) but not in MI.

Conclusions: 1) Heterogeneity in conduction and repolarization evolve differently as MI heals. 2) The CHI provides a summary of heterogeneity of conduction. 3) ART cannot estimate ERP in MI presumably because of post-repolarization refractoriness.